

## CLAIMS

1. A vaccine composition comprising a mammalian prion protein and an adjuvant eliciting a humoral immune response.
2. The composition of claim 1, wherein the prion protein is a member of the group consisting of human, bovine, deer, elk, and sheep prion protein.
3. The composition of claim 2, wherein the prion protein comprises an amino acid sequence which is a member of the group consisting of residues 90-144 of SEQ ID NO:1; residues 112-214 of SEQ ID NO:1; residues 93-156 of one of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4 or SEQ ID NO:8; and residues 123-225 of one of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, or SEQ ID NO:8.
4. The composition of claim 3, wherein all amino acid residues are D-amino acids.
5. The composition of claim 1, wherein the prion protein comprises at least one homolog of residues 90-144 of SEQ ID NO:1 wherein at least one of residues 121, 122, 128, 129, and 130 has been substituted with Pro, Asp, Glu, Lys, Gly, Ser or Cys.
6. The composition of claim 5, wherein all amino acids of the homolog are D-amino acids.
7. The composition of claim 5, wherein the prion protein further comprises an N- or C-terminal sequence of 4-10 Lys or Asp residues.
8. The composition of claim 6, wherein the prion protein comprises both an N-terminal and a C-terminal sequence of 4-10 Lys or Asp residues.
9. The composition of claim 1, wherein the adjuvant is cholera toxin subunit B (CT-B), heat-labile enterotoxin (LT) or aluminum hydroxide.

10. The composition of claim 9, wherein the prion protein is covalently attached to the cholera toxin subunit B.
11. A method of preventing or treating a prion disease, comprising mucosal administration of the vaccine of claim 1 to a mammalian subject in need thereof.
12. The method of claim 11, wherein the mammalian subject is a member of the group consisting human, bovine, deer, elk, and sheep.
13. The method of claim 11, wherein the mucosal administration is a member selected from the group consisting of oral, intragastric, intranasal, rectal and intraocular administration.
14. The method of claim 11, wherein the subject is human and the prion disease is a member selected from the group consisting of Creutzfeldt-Jakob's Disease, variant Creutzfeldt-Jakob's Disease, Gerstmann-Sträussler-Scheinker disease, prion protein-conophilic angiopathy, and familial fatal insomnia.
15. The method of claim 11, wherein the subject is bovine and the prion disease is bovine spongiform encephalopathy.
16. The method of claim 11, wherein the subject is deer or elk and the prion disease is chronic wasting disease.
17. The method of claim 11, wherein the subject is sheep and the prion disease is scrapie.
18. The method of claim 11, further comprising repeating the mucosal administration at least once.
19. The method of claim 18, comprising repeating the mucosal administration within one month after the first administration.

20. A vaccine composition comprising an attenuated *Salmonella typhi* bacterium transfected spp strain transformed with a vector capable of expressing a mammalian prion protein.
21. The composition of claim 20, wherein the mammalian prion protein is a member of the group consisting of human, bovine, deer, elk, and sheep prion protein.
22. The composition of claim 21, wherein the prion protein comprises an amino acid sequence which is a member of the group consisting of residues 90-144 of SEQ ID NO:1, and residues 93-156 of one of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:8.
23. The composition of claim 22, wherein all amino acid residues are D-amino acids.
24. The composition of claim 20, wherein the prion protein comprises at least one homolog of residues 90-144 of SEQ ID NO:1 wherein at least one of residues 121, 122, 128, 129, and 130 has been substituted with Pro, Asp, Glu, Lys, Gly, Ser or Cys.
25. The composition of claim 24, wherein all amino acids of the homolog are D-amino acids.
26. The composition of claim 24, wherein the prion protein further comprises an N- or C-terminal sequence of 4-10 Lys or Asp residues.
27. The composition of claim 24, wherein the prion protein comprises both an N-terminal and a C-terminal sequence of 4-10 Lys or Asp residues.
28. The composition of claim 20, wherein the *Salmonella* spp strain is of a strain selected from *Salmonella typhimurium* LVR01, LVR03 and SL3261, *Salmonella enteritidis* LVR02, and *Salmonella typhi* CVD915.

29. A method of preventing or treating a prion disease, comprising mucosal administration of the vaccine of claim 20 to a mammalian subject in need thereof.
30. The method of claim 29, wherein the mammalian subject is a member of the group consisting human, bovine, deer, elk, and sheep.
31. The method of claim 29, wherein the mucosal administration is a member selected from the group consisting of oral, intragastric, intranasal, rectal and intraocular administration.
32. The method of claim 29, wherein the subject is human and the prion disease is a member selected from the group consisting of Creutzfeldt-Jakob's Disease, variant Creutzfeldt-Jakob's Disease, Gerstmann-Sträussler-Scheinker disease, prion protein-congophilic angiopathy, and familial fatal insomnia.
33. The method of claim 29, wherein the subject is bovine and the prion disease is bovine spongiform encephalopathy.
34. The method of claim 29, wherein the subject is deer or elk and the prion disease is chronic wasting disease.
35. The method of claim 29, wherein the subject is sheep and the prion disease is scrapie.
36. The method of claim 29, further comprising repeating the mucosal administration at least once.
37. The method of claim 36, comprising repeating the mucosal administration within one month after the first administration.
38. A pharmaceutical composition comprising a mammalian prion protein, an adjuvant eliciting a humoral immune response, and a pharmaceutically acceptable excipient.

39. The composition of claim 38, wherein the excipient is sodium bicarbonate or alum.
40. A method for preventing prion disease comprising administering a priming dose of the pharmaceutical composition of claim 38 by an intradermal, subcutaneous, intramuscular, or intravenous route, and subsequently administering a booster dose of the pharmaceutical composition by an oral, nasal, intragastric, rectal, or intraocular route.
41. The composition of claim 1, wherein the prion protein comprises at least one homolog of residues 112-214 of SEQ ID NO:1 wherein at least one of residues 112, 116, 117, 118, 121, 122, 128, 129, and 130 has been substituted with Pro, Asp, Glu, Lys, Gly, Ser or Cys.
42. The composition of claim 41, wherein all amino acids of the homolog are D-amino acids.
43. The composition of claim 41, wherein the prion protein further comprises an N- or C-terminal sequence of 4-10 Lys or Asp residues.
44. The composition of claim 42, wherein the prion protein comprises both an N-terminal and a C-terminal sequence of 4-10 Lys or Asp residues.
45. The composition of claim 21, wherein the prion protein comprises an amino acid sequence which is a member of the group consisting of residues 112-214 of SEQ ID NO:1, and residues 123-225 of one of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:8.
46. The composition of claim 45, wherein all amino acid residues are D-amino acids.
47. The composition of claim 20, wherein the prion protein comprises at least one homolog of residues 112-214 of SEQ ID NO:1 wherein at least one of residues 112, 116, 117, 118, 121, 122, 128, 129, and 130 has been substituted with Pro, Asp, Glu, Lys, Gly, Ser or Cys.

48. The composition of claim 47, wherein all amino acids of the homolog are D-amino acids.
49. The composition of claim 47, wherein the prion protein further comprises an N- or C-terminal sequence of 4-10 Lys or Asp residues.
50. The composition of claim 48, wherein the prion protein comprises both an N-terminal and a C-terminal sequence of 4-10 Lys or Asp residues.